Systolic Click and Late Systolic Murmur

INFORMATION ON SYSTOLIC CLICKS and late systolic murmurs was at a virtual standstill for half a century after Gallavardin's description in 1913 when he related systolic clicks to pericardial adhesions found at necropsy. Since systolic clicks often (but not invariably) introduce late systolic murmurs, and since the physiologic mechanisms of systolic murmurs proposed in the mid to late 50's did not explain murmurs confined to late systole, both of these auscultatory events continued to be regarded as "extracardiac."[1] The systolic whoop or honk, described by Osler in 1880, was not even remotely considered in the same context.[2] In the early 1960's, isolated late systolic murmurs as well as clicks with late systolic murmurs were attributed to mitral regurgitation. This was a major step forward.[1] New data then began to accumulate, at first slowly, then in the last few years, logarithmically. We are now faced with an information explosion over what for nearly 50 years lay dormant as an innocent auscultatory curiosity. It is therefore timely for THE WESTERN JOURNAL OF MEDICINE to publish a specialty conference on this topic.

The 1960's introduced what might be called the "leaflet-chordal" phase of our knowledge of clicks and late systolic murmurs. Left ventricular angiocardiography convincingly showed systolic prolapse of the posterior mitral leaflet together with mitral regurgitation.[1] Response of the late systolic murmur to vasoactive drugs (amyl nitrate and pressor agents) was sufficiently similar to the response of the holosystolic murmur of mitral regurgitation to lend weight to the angiocardiographic conclusions. The technical capability of recording sound from within the heart, especially the left heart, permitted localization of both the clicks and late systolic murmurs to the left atrium, a site appropriate for origin due to an incompetent mitral valve.[3] Left ventricular cineangiography recorded simultaneously with cine-trace phonocardiograms allowed precise timing of clicks and late systolic murmurs, and clearly showed that mitral regurgitation started in late systole. Prolapse of the mitral valve was ascribed to leaflet-chordal redundancy which permitted early systolic competence but caused late systolic overshoot. The clicks were ascribed to abrupt tensing of the elongated chordae and redundant leaflet tissue (chordal snaps). Other mechanisms were not entertained at that time.

A general interest in auscultatory responses to *physical* maneuvers became popular as clinicians sought more practical alternatives to the administration of amyl nitrite or pressor agents. Valsalva's maneuver, squatting, prompt standing and isometric exercise (hand grip) were applied with advantage to patients with isolated clicks and clicks with late systolic murmurs. The response not only increased the diagnostic yield in such patients, but in some served to provoke systolic whoops or honks, indicating that the auscultatory spectrum included clicks, late systolic murmurs as well as the high pitched musical whoop.

Careful phonocardiographic study of the response to physical and pharmacologic interventions showed that the click and late systolic murmur migrated toward or away from the first heart sound as left ventricular volume decreased or increased. Accordingly, the mid to late systolic click could be made to appear in early systole and the late systolic murmur seriatim became holosystolic or nearly so. It was then shown that spontaneous occurrence of early systolic clicks occasionally introduced long systolic murmurs. It became necessary to distinguish systolic clicks of mitral origin from ejection sounds of semilunar valve or great vessel origin.

The next stage in our knowledge can be designated the "myocardial phase." Apex or kinetocardiograms in patients with clicks and late systolic murmurs sometimes recorded bifid left ventricular impulses;[2] shortly thereafter, left ventricular cineangiograms established the presence of contraction abnormalities of the left ventricle. Initial observations on inferior wall abnormalities were extended to include posteromedial contraction with anterior convexity, ring-like contraction of the mid portion of the left ventricle, inadequate long axis shortening, posterior akinesis and cavity obliteration similar to that seen in hypertrophic obstructive cardiomyopathy (idiopathic hypertrophic subaortic stenosis).[4] The degree of contraction abnormality ranges from hypokinesis to frank dyskinesis, and has prompted some investigators to designate the click-late systolic murmur

complex as a segmental cardiomyopathy that throws the chordae and leaflets into a slack position allowing late systolic prolapse of the mitral valve.[5] However, it is difficult to know which comes first; do redundant chordae and leaflets result in segmental abnormalities of left ventricular contraction or vice versa?

Up to this point, a left ventricular angiocardiogram was the final arbiter in providing precise diagnostic information. Phonocardiograms and apex or kinetocardiograms were useful but indirect noninvasive tools. *Echocardiography* was ideally suited for the direct study of the click-late systolic murmur complex since it provided safe, painless, noninvasive information; could be repeated easily and frequently, and could define precisely movements of the mitral leaflets. It is no wonder that the number of diagnosed cases has risen precipitously because of liberal use of echocardiograms and investigation has flourished.[6] Mitral leaflet motion can now be defined in previously ambiguous instances of isolated systolic clicks without late systolic murmurs, and echocardiographic recordings can be made after provocative tests such as amyl nitrite inhalation. Relatives of propositi can be studied, shedding light on familial incidence. In addition, echocardiography has provided further anatomic information. Since the ultrasound beam is most precise and reproducible in recording anterior mitral leaflet motion, it is not surprising that a relatively high incidence of *anterior* as well as posterior leaflet prolapse was found. More recently, left ventricular angiocardiography has confirmed frequent prolapse of either or both mitral leaflets and, in addition, right ventricular angiography has disclosed asynergy of that chamber as well as tricuspid leaflet prolapse.[4] During the course of such studies, coronary cineangiography has generally shown normal vessels, but more recently, coronary arterial abnormalities have been described, including corkscrew appearance of major vessels or their branches, short main left coronary artery and anomalous origin of the right coronary artery.[4] The significance of these observations is not yet clear.

The clinical aspects of the click-late systolic murmur complex have expanded in parallel with the anatomic and physiologic information cited here. At one end of the spectrum are persons with neither clicks nor late systolic murmurs but with echocardiographic evidence of mitral leaflet prolapse. Starting at this point, the clinical scope broadens considerably to include a variety of features in the physical signs, chest x-ray studies, history and electrocardiograms, as well as a number of significant complications and associations with other cardiac diseases.[2]

The auscultatory hallmarks—mid to late systolic clicks and late systolic murmurs—may be absent, intermittent, present individually or in combination, variably accompanied by systolic whoops or honks and influenced by a variety of physical or pharmacologic interventions. Palpation of the left ventricular impulse may be normal or may detect a double (bifid) systolic impulse recalling but not necessarily paralleling the abnormal contraction patterns seen on left ventricular angiocardiography. Physical appearance and x-ray films of the chest show relatively frequent thoracic bony abnormalities, especially loss of thoracic kyphosis (straight back), decreased anteroposterior chest diameter, scoliosis and pectus excavatum. It is not yet clear whether these abnormalities are independent of or formes frustes of Marfan's syndrome in which unusually long chordae tendineae, laxity of mitral valve tissue and clicks and late systolic murmurs have been found.[7]

The electrocardiographic abnormalities initially emphasized were T wave inversions in inferior leads, but the range has considerably increased. Rhythm disturbances vary from occasional atrial or ventricular premature beats to supraventricular tachycardia, atrial fibrillation and ventricular tachycardia. Arrhythmias may occur at rest, but exercise testing has been used to provoke occult arrhythmias or to determine the extent to which physical exertion aggravates them. Sudden death (mentioned later) has been attributed to arrhythmias. Inverted T waves are not confined to inferior leads but appear in lateral precordial leads and are occasionally accompanied by ST segment abnormalities. QT prolongation has been reported, but no relationship has been established between QT prolongation, ventricular arrhythmias, deafness and sudden death in these patients. In addition, sinus bradycardia, and first, second or complete heart block has been mentioned.

The history is important in several respects. Female prevalence of the click-late systolic murmur syndrome approaches 80 percent. Familial occurrence is well established and now easy to document because of echocardiography. Mild fatigue and dyspnea are often present without acceptable physiologic explanation. A high inci-

dence of psychological disorders has been described, but the prevalence and significance of such disorders are unknown. Despite the frequency of arrhythmias, syncope or presyncopal symptoms are exceptional. In addition, chest pain is a relatively common complaint. The pain is almost always atypical in quality, location, duration and relation to exercise; the pain only rarely resembles angina, is generally mild but occasionally incapacitating, occurs with angiographically normal coronary arteries and is unassociated with chest wall tenderness. The authors of the Specialty Conference call attention to their own work which has shown that the atypical chest pain can be reproduced by elevating systemic arterial and left ventricular systolic pressures with intravenously administered phenylephrine.[8] If the pain originates from regional discrepancies between oxygen supply and demand (papillary muscles, contraction abnormalities), then an increase in left ventricular wall tension with phenylephrine could provoke or aggravate this discrepancy. It may be noteworthy in this regard that propranolol therapy has met with some measure of success in relieving the chest pain although these results are inconclusive.

There are three important complications of the click-late systolic murmur syndrome. Sudden death is the most dramatic and widely heralded.[9] The cause has not been established but a relationship among sudden death and arrhythmias, abnormalities of left ventricular wall motion and familial occurrence is commented upon in the Specialty Conference. The incidence of sudden death is unknown, but all evidence indicates that prevalence is very low. The second important complication of the click-late systolic murmur syndrome is infective endocarditis. This comes as no surprise in view of the known susceptibility of incompetent mitral valves to infection. It has also been shown that infective endocarditis can develop in patients with isolated clicks, *no* late systolic murmur and presumably no mitral regurgitation, although the degree of susceptibility in this context has not been established. The third complication is rupture of chordae tendineae which can understandably follow infective endocarditis, but interestingly, may occur spontaneously.

The systolic click-late systolic murmur occurs not only in the setting discussed above, but occasionally in association with other cardiac diseases. Comment has already been made on clicks, late systolic murmurs and mitral regurgitation in Marfan's syndrome.[7] Mitral valve prolapse has also been documented in otherwise uncomplicated ostium secundum atrial septal defect.[10] Such patients may or may not have clicks and late systolic murmurs. Because of this association, it is desirable that all patients with secundum atrial septal defects have mitral valve echocardiograms. Clicks, late systolic murmurs and mitral valve prolapse have been described in coronary artery disease and related to systolic prolapse caused by papillary muscle dysfunction.[11] In idiopathic hypertrophic subaortic stenosis (hypertrophic obstructive cardiomyopathy) there is characteristic systolic anterior movement of the anterior mitral leaflet after initial closure. Late systolic mitral regurgitation is common and has been held accountable for the occasional resemblance of the systolic murmur to mitral leaflet prolapse. In addition, midsystolic clicks have been observed in idiopathic hypertrophic subaortic stenosis, but the incidence must be very low and the mechanism is unclear.

We do not yet know whether the systolic click and late systolic murmur information explosion has passed its peak. However, it is likely that lively interest in this topic will continue for some time.

JOSEPH K. PERLOFF, MD
Professor of Medicine and Pediatrics
Chief, Cardiocascular Section
University of Pennsylvania School of Medicine
Philadelphia

REFERENCES

1. Barlow JB, Pocock WA, Marchand P, et al: The significance of late systolic murmurs. Am Heart J 66:443-452, 1963

2. Perloff JK, Roberts WC: The mitral apparatus—Functional anatomy of mitral regurgitation. Circulation 41:227-239, 1972

3. Ronan JA, Perloff JK, Harvey WP: Systolic clicks and the late systolic murmur—Intracardiac phonocardiographic evidence of their mitral valve origin. Am Heart J 70:319-325, 1965

4. Scampardonis G, Yang SS, Maranhao V, et al: Left ventricular abnormalities in prolapsed mitral leaflet syndrome. Circulation 48:287-297, 1973

5. Gulotta SJ, Gulco L, Padmanabhan V, et al: The syndrome of systolic click, murmur and mitral valve prolapse—A cardiomyopathy? Circulation 49:717-728, 1974

6. DeMaria AN, King JF, Bogren HG, et al: The variable spectrum of echocardiographic manifestations of the mitral valve prolapse syndrome. Circulation 50:33-41, 1974

7. Edwards JE: Mitral insufficiency resulting from "overshooting" of leaflets. Circulation 43:606-612, 1971

8. LeWinter MM, Hoffman JR, Shell WE, et al: Phenylephrine-induced atypical chest pain in patients with prolapsing mitral valve leaflets. Am J Cardiol 34:12-18, 1974

9. Shappell SD, Marshall CE, Brown RE, et al: Sudden death and the familial occurrence of mid-systolic click, late systolic murmur syndrome. Circulation 48:1128-1134, 1973

10. McDonald A, Harris A, Jefferson K, et al: Association of prolapse of posterior cusp of mitral valve and atrial septal defect. Br Heart J 33:383-387, 1971

11. Steelman RB, White RS, Hill JC, et al: Mid systolic clicks in arteriosclerotic heart disease. Circulation 44:503-515, 1971